

## REMARKS

Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow.

### **I. Status of the Claims**

No claim amendments are made in this response. Claims 1-3, 5-35, 37, 39, 41 and 43-45 are under examination, with claims 46-52, 54-82 and 84-123 withdrawn from consideration. Because the withdrawn claims are directed to a process of making and using the product, Applicants respectfully request rejoinder of the process claims upon allowance of the product claims.

### **II. Rejection of Claims under 35 U.S.C. §103(a)**

#### **A. Liversidge and Straub**

Claims 1-4, 6, 8-24, 26-30, 32-35, 37, 39, 41 and 43-45 are rejected under 35 U.S.C. §103(a) for alleged obviousness over U.S. Patent No. 6,267,989 to Liversidge ("Liversidge") in view of U.S. Patent Application Publication No. 2002/0142050 by Straub et al. ("Straub"). Applicants respectfully traverse the rejection.

Liversidge describes reducing a nanoparticulate active agent composition to an effective average particle size which is effective at preventing crystal growth in the nanoparticulate active agent composition. Although additional adjuvants, such as preserving, wetting, emulsifying and dispensing agents, may be added to Liversidge's nanoparticulate active agent composition, Liversidge cautions that the addition of other substances may affect crystal growth. *See* column 10, lines 23-26, and column 3, lines 6-16.

Liversidge distinguishes his invention from the prior art that requires the additional substances to prevent crystal growth. *See* column 3, lines 10-16. Moreover, nothing in

Liversidge suggests that his method of reducing crystal growth with small particle size is in anyway insufficient, non-functional, or requires further improvement: “nanoparticulate [active agent] compositions having an optimal effective average particle size exhibit minimal particle aggregation and crystal growth, even following prolonged storage periods or exposure to elevated temperatures” (Liversidge, column 3, lines 36-40).

As such, the Examiner’s suggestion to add the crystal growth inhibitor sugars of Straub’s to the composition of Liversidge’s is without reason and contravenes the teachings of Liversidge. That is, one of ordinary skill in the art would not have any reason to add a crystal growth inhibitor (Straub’s sugars) to Liversidge’s composition because 1) Liversidge has already solved the problem of crystal growth and Liversidge recommends against adding other substances to the composition for the concerns of side effects and increased cost.

The Examiner’s reasons to add the sugars in Straub to the composition of Liversidge were that such an addition would result in an “additive effect” and/or “prolonged” stability. The Examiner asserted that “one of ordinary skill in the art would have been motivated to combine surface modifiers, mannitol as an anti-crystallization [agent], and nanoparticle drug with the expectation of [obtaining an] *additive* affect [*sic*, effect] in preventing crystal growth in nanoparticulate composition [and] to obtain a nanoparticulate composition that exhibit[s] *prolonged* particle size stability even following exposure to elevated temperatures” (final Office Action, page 3, lines 11-15; emphasis added) lacks any factual basis. There is nothing on record, in the prior art, or asserted to be within the knowledge of one of ordinary skill in the art of to support the Examiner’s assertion, that combining the teachings of Liversidge and Straub will result in an “additive effect” or “prolonged” stability.

In view of the foregoing, Applicants respectfully request withdrawal of the rejection.

**B. Liversidge, Straub and Liversidge '049'**

Claims 25, 30-35, 37, 39, 41 and 43-45 are rejected under 35 U.S.C. §103(a) for alleged obviousness over Liversidge, Straub and U.S. Patent Application Publication No. 2005/0004049 ("Liversidge '049"). Applicants respectfully traverse the rejection.

Liversidge and Straub are discussed supra. Liversidge '049 is cited for the alleged teaching of a bioadhesive composition. Liversidge '049 fails to cure the deficiencies of Liversidge and Straub argued above.

Each of the claims at issue ultimately depends from claim 1. Since, as discussed above, claim 1 is non-obvious over the cited art, it follows that claims 25, 30-35, 37, 39, 41 and 43-45 likewise are non-obvious for the same reason. Therefore, Applicants respectfully request withdrawal of the rejection.

**C. Bagchi, De Garavilla and Straub**

Claims 1-6, 8-10, 12, 14-15, 17, 21-24, 26-30 and 32-45 are rejected under 35 U.S.C. §103(a) for alleged obviousness over U.S. Patent No. 5,665,331 to Bagchi et al. ("Bagchi") in view of U.S. Patent No. 5,834,025 to De Garavilla et al. ("De Garavilla") and Straub. Applicants respectfully traverse the rejection.

Applicants previously responded that one skilled in the art would not have had any reason to substitute Bagchi's crystal growth modifier, which must possess at least 75% identity in chemical structure to the active agent, for either glycerol as taught by De Garavilla or mannitol as taught by Straub.

The Examiner's response to the Applicants argument that there is no reason to combine the references is that because no specific active agent is recited in the base claim, the combined teachings of Bagchi and De Garavilla or Straub could read on Applicants' claims. This statement

does not address Applicants' argument. Applicant is not arguing that when combined, the references fail to teach the limitations of the base claims. Rather, the Applicant demonstrated that there is no reason to combine Bagchi and De Garavilla or Straub in the first instance.

More specifically, Bagchi describes a laundry list of active agents at column 5, lines 27-55. The Examiner has failed to establish that glycerol or mannitol shares at least 75% identity with any of the listed active agents of Bagchi. Moreover, one skilled in the art would not have immediately envisaged that glycerol or mannitol shares the required structural similarities with the active agents of Bagchi. Therefore, a reason or motivation to combine the cited references is lacking.

Accordingly, the Examiner has failed to establish a prima facie case of obviousness and therefore, withdrawal of the rejection is warranted.

CONCLUSION

The present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested. The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by the credit card payment instructions in EFS-Web being incorrect or absent, resulting in a rejected or incorrect credit card transaction, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

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